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The impact of an individualized risk-adjusted approach on hypertension treatment in primary care

Different approaches on hypertension treatment

Stefan Zechmann^{1*}, MD, Oliver Senn¹, MD, Fabio Valeri¹, Stefan Neuner-Jehle¹, MD, Thomas Rosemann¹, MD, PhD, Sima Djalali¹, MD and the FIRE study group

¹Institute of Primary Care, University of Zurich, University Hospital Zurich, Zurich, Switzerland

*Corresponding author:

Stefan Zechmann

Institut für Hausarztmedizin

UniversitätsSpital Zürich

Pestalozzistrasse 24

CH-8091 Zürich

phone: +41 (0) 44 / 25598 55

Fax: +41 (0) 44 / 255 90 97

stefan.zechmann@usz.ch

Abstract

Previous studies suggest that up to 60% of all patients with hypertension receive inappropriate treatment. Current 2013 ESH/ESC guideline recommend taking cardiovascular risk factors into account whenever assessing treatment of patients with hypertension. We hypothesize this approach will reduce the proportion of patients receiving inappropriate treatment. In this cross-sectional study using electronic medical records of Swiss primary care patients we estimate the proportion of patients receiving inappropriate treatment using two approaches 1.) based on a blood pressure threshold of 140/90 mmHg 2.) based on cardiovascular risk factors. We identified 22'434 patients with hypertension. Based on these approaches, 72.7% and 44.6% respectively qualified for drug treatment. 23.0% and 10.8% respectively received inappropriate treatment. Application of the 2013 ESH/ESC guideline reduced the proportion of patients receiving inappropriate treatment by 50%. This shows the major impact of risk-adjustment and highlights the need for a patient centered approach in hypertension treatment.

Introduction

Elevated blood pressure (BP) is a leading risk factor for premature death, stroke and heart disease worldwide (1-3). A broad armament of evidence-based treatment options as well as guidelines providing the latest evidence on how to use these different treatment options exist (3-7). Nevertheless, there is a suspicion that a considerable proportion of patients diagnosed with hypertension worldwide do not receive an appropriate treatment. Different studies found a substantial gap between guideline recommendations and the actual treatment of patients with hypertension (8-15). This gap is often referred to as evidence-performance gap (EPG) (16, 17). 60% or more patients with hypertension worldwide, especially patients treated in primary care settings, might be affected by the EPG. These previous studies used the BP threshold of 140/90 mmHg as a single criterion for appropriate treatment. Consequently, all patients with a BP of 140/90 mmHg or above without treatment, disregarding their overall cardiovascular risk (CVR), were defined as being affected by the EPG.

As comorbidities and other CVR factors besides hypertension are frequent in real-life patients, especially in the primary care setting, the integration of comorbidities and CVR factors into the assessment is of greatest importance (18-21).

Recent studies support the recommendation to shift focus from rigid BP thresholds to patients' overall CVR to facilitate an individualized risk-adjusted assessment whenever deciding on hypertension treatment. A possible explanation for the EPG is that primary care physicians' (PCP) adapt guideline recommendations to the needs of their real life patients, a finding that has been shown e.g. in diabetes management (22). Thus, EPGs might be rather explained by an individualized risk-adjusted assessment than by low adherence to guidelines (23).

The latest guideline of the European Society of Hypertension (ESH) and the European Society of Cardiology (ESC) published in 2013 recommends a broader and more individualized approach whenever assessing treatment options of patients with hypertension. This new risk-adjusted approach takes other CVR factors, patients' age and frailty into account (24, 25). At present, the 2013 ESH/ESC guideline is the clinical standard for the management of patients with hypertension in Europe.

However, the proportion of patients with hypertension qualifying for treatment according to this guideline remains unknown, as it is true for the proportion of patients affected by the EPG.

We hypothesize that the risk-adjusted approach will result in a smaller proportion of patients qualifying for treatment. Thus, the EPG will decrease.

Methods

This cross-sectional study used data collected from electronic medical records of primary care patients with hypertension registered between January 2009 and August 2015. We estimated the proportion of patients qualifying for treatment according to two different approaches and assessed whether PCPs had prescribed treatment or not. Primary outcome of the study was the proportion of patients who did not receive treatment although recommended by guidelines. By definition, these patients were considered as being affected by an EPG. Secondary outcome was the difference between the EPG estimations obtained by the two approaches.

First, patients were stratified according to the BP threshold of 140/90 mmHg, subsequently referred as « standardized BP approach». Second, patients were stratified to CVR categories according to BP levels and additional CVR factors as recommended in the 2013 ESH/ESC guideline, subsequently referred as «risk-adjusted approach» (24, 25).

Data collection

Medical record data were extracted from the database of the «Family medicine ICPC Research using Electronic medical records» (FIRE) project. FIRE is an ongoing research project of the Institute of Primary Care at the University and University Hospital of Zurich, Switzerland, involving PCPs in the German speaking part of Switzerland. PCPs voluntarily provide standardized, anonymized medical record data of all patient encounters in daily practice. Data cover patients' demographics, vital signs, diagnostic codes using the second version of the International Classification of Primary Care (ICPC-2) (26, 27), laboratory values and data on medication using the Anatomical Therapeutic Chemical Classification System (ATC) (28). Further details on the FIRE database and its validation are provided elsewhere (21, 29).

Patients

All patients registered in the FIRE database between January 2009 and August 2015 were assessed for the eligibility criterion hypertension.

Definition of hypertension was based on the occurrence of at least one of the following criteria (which were searched for in the following hierarchically order):

- more than two BP measurements $\geq 140/90$ mmHg or
- at least one recorded ICPC-2 coding (K85 «elevated blood pressure», K86 «hypertension uncomplicated», K87 «hypertension complicated») or
- at least two prescriptions of antihypertensive drugs according to ATC coding as validated by Lamers et al. (30) (C02 «antihypertensives», C03A «low-ceiling diuretics, thiazides», C03EA01 «hydrochlorothiazide and potassium-sparing agents», C07 «beta blocking agents», C08 «calcium channel blockers», C09A «ace inhibitors, plain», C09B «ace inhibitors, combinations») and additionally ATC coding of angiotensin-II-receptor antagonists (C09C «angiotensinogen II antagonists, plain», C09D «angiotensinogen II antagonists, combinations»).

Exclusion criteria:

Patients with less than two blood pressure measurements (regardless of the measured value; this was possible as eligible patients had to meet only one and not all three inclusion criteria to be eligible), less than two PCP consultations, age below 18 years or pregnancy were excluded.

Patients individual observation period was defined using an inclusion and an end date. The first visit date a patient met one of the three inclusion criteria was used as inclusion date. End date was the date of the latest visit a BP measurement was made. ICPC-2 codes were used if they occurred only once as these codes were based on best medical practice by participating PCPs who did the coding by themselves. ATC codes were used if they occurring at least twice to avoid prescription errors. We used the latest available data for changing parameters (e.g. laboratory data or demographic data such as weight) looking backwards starting at the end date.

Baseline characteristics

The following baseline characteristics of included patients were assessed based on medical record entries: «age», «antihypertensive drugs», «concomitant non-antihypertensive drugs», «concomitant chronic diseases», «BP measurements», «risk factors» and «asymptomatic organ damage». Patients' chronic comorbidities were assessed based on the ICPC-2 classification as recommended by O'Halloran et al. (31) and based on PCGs (30).

Stratification according to BP levels («standardized BP approach»)

We established five hypertension grade groups: «normal» (systolic blood pressure (SBP) ≤ 129 mmHg and diastolic blood pressure (DBP) ≤ 84 mmHg), «high normal» (SBP 130–139 mmHg, DBP 85–89 mmHg), «grade 1» (SBP 140–159 mmHg, DBP 90–99 mmHg), «grade 2» (SBP 160–179 mmHg, DBP 100–109 mmHg), «grade 3» (SBP ≥ 180 mmHg, DBP ≥ 110 mmHg) (24).

Patients were stratified to these groups based on the mean value of all recorded BP measurements. As recommended by the 2013 ESC/ESH guideline, stratification to a specific hypertension grade group was based on the higher level, no matter if this concerned the SBP or the DBP. If two BP measurements were available from the same visit, we used the mean of the two available values.

Stratification according to CVR categories («risk-adjusted approach»)

As recommended by the 2013 ESH/ESC guideline, we established eight CVR categories: «average», «low», «low-moderate», «moderate», «moderate-high», «high», «high-very high», and «very high» depending on patients' hypertension grade group and number of existing risk factors, asymptomatic organ damage and established diseases (see Fig 1. for details). Therefore, we searched each patient's latest medical record for ICPC-2 diagnoses, medication lists/ATC codes and laboratory results. (Table 1)

Fig 1. stratification of patie

Table 1.

Treatment criteria

All patients stratified to hypertension grade group «grade ≥ 1 » qualified for drug treatment according to the «standardized BP approach».

All patients with hypertension grade group «grade ≥ 1 » having a CVR category of at least «high» qualified for drug treatment according to the risk-adjusted approach.

Exceptions within the risk-adjusted approach apply to young patients with isolated systolic hypertension (ISH) and elderly patients. In the context of ISH, an age of 30 years or below is determined as «young» (32). We therefore decided to consider patients aged ≤ 30 years with a mean SBP level of >140 mmHg and a mean DBP level of <90 mmHg as patients affected by ISH. In regard to age, neither the 2013 ESH/ESC guideline nor general medical literature defines exact thresholds for «elderly» (24, 25, 33-35).

Thus, we refrained from setting an exact age threshold and decided to stratify patients affected by the EPG according to age.

In order to assess possible changes in clinical practice over the observation period of 6 years we performed a sensitivity analysis comparing patients within the first three years to patients within the last three years. As eligible patients could be found anytime between 01.01.2009 and 31.12.2015 and duration of patients' observation period was subject to change, patients included in the first as well as the last years were not included in this sensitivity analysis.

Statistical analysis

Continuous variables are presented as means and standard deviations (SD), categorical data as frequencies and percentages. We used Walds' interval to calculate the confidence interval (CI) (36). Data analysis was performed using R ® Statistics software (version 3.2.0).

Results

Until August 2015, 264'641 primary care patients were registered in the FIRE database. All patients were assessed for the eligibility criterion hypertension and 48'602 were defined as eligible. Of these, 20'236 patients were excluded since they had less than two BP measurements available, 312 patients had less than two PCP consultations, 5'613 patients were below the age of 18 years and 7 patients were pregnant. Data of the remaining 22'434 patients with hypertension were included in the analysis (Fig. 2).

Included patients were on average 66.4 years old, and 50.7% were male. The average observation period for the individual patient was 2.7 years. During observation, on average 9.7 BP measurements per patient were performed, corresponding to an average of 3.7 BP measurements per patient per year. Besides hypertension, patients had a mean of 4.8 concomitant chronic diseases and took 5.9 concomitant non-antihypertensive drugs. Detailed baseline characteristics are depicted in Table 2.

Fig 2. inclusion flowchart v2

Table 2.

«Standardized BP approach»

Based on the BP threshold of 140/90 mmHg, 72.7% (95% CI, 72.0 to 73.4) of all patients qualified for drug treatment.

49.7% (95% CI, 48.8 to 50.1) received a drug as recommended, while 23.0% (95% CI, 21.8 to 24.1) received no drug although qualifying for treatment. The latter were therefore identified as being affected by the EPG (Fig. 3).

Fig 3. Patients with hypertens

«Risk-adjusted approach»

Based on the CVR categories, 44.6% (95% CI, 43.6 to 45.6) of all patients qualified for drug treatment. 33.9% (95% CI, 32.8 to 34.9) received a drug as recommended, while 10.8% (95% CI, 9.5 to 12.0) received no drug although qualifying for treatment. The latter were therefore identified as being affected by the EPG (Fig. 3).

Difference between approaches

The proportion of patients affected by the EPG differed by 12.2% (95% CI, 10.9 to 13.4) depending on the approach used.

Further analysis

The stratification of all patients to the 8 different CVR categories showed that 53.2% (11'941/22'434) of all patients were assigned to the «moderate-high» or to a lower CVR category. Accordingly, 46.8% (10'493/22'434) were assigned to higher CVR categories, but only 8.1% (1'816/22'434) were assigned to the «very high» CVR category. Results of stratification of patients to different CVR categories are depicted in fig. 1.

The age-stratification of all 2'416 patients affected by the risk-adjusted EPG approach showed that 11.1% (266/2'416) of these patients were 60 years or younger while 88.9% (2'150/2'416) were older than 60 years.

Among patients younger than 60 years, 3 patients were identified as patients affected by ISH (Fig. 4).

Fig 4. Age stratification

Sensitivity analysis splitting the six-year observation period into two blocks of three years each showed no relevant difference in clinical practice concerning our main outcome of “appropriateness of hypertension treatment”.

Discussion

In this study, we applied two different approaches to data of patients with hypertension treated in Swiss primary care to evaluate the proportion of patients qualifying for treatment and being affected by an EPG. That way, we were able to demonstrate the actual impact of an individualized risk-adjustment compared to an assessment based on a rigid BP threshold.

Using the «standardized BP approach», the proportion of patients with hypertension qualifying for drug treatment was 72.7% compared to 44.6% using the «risk-adjusted approach», resulting in a difference of 28.1%. The proportion of patients identified as being affected by the EPG decreased from 23.0% using the «standardized BP approach» to 10.8% using the «risk-adjusted approach», resulting in a difference of 12.2%.

Our results using the «standardized BP approach» are comparable to previous studies that only used the «standardized BP approach» and neglected patients' individual CVR factors. Some of these studies described a decrease of the EPG over time but assumed many reasons such as a healthier lifestyle, increase of drug treatment or higher awareness of hypertension (10, 11, 13, 14, 37, 38).

Scheltens et al. were the first and only authors using a more individualized approach estimating the EPG in hypertension management based on the Framingham risk function (12). However, they applied this approach only to a small (n=292) and special subgroup of patients with hypertension who were free

from cardiovascular disease and had an average age of 38 years. Moreover, this approach was based on a number of assessment criteria that must be considered outdated to date (12).

Just recently, Navar-Boggan et al. demonstrated that the introduction of a new guideline for hypertension management in the United States changed the proportion of patients qualifying for treatment significantly (39).

Applying the 2013 ESH/ESC guideline we are now the first using a risk-adjusted approach. This risk-adjusted approach reduced the EPG by more than 50%. A more detailed analysis of the proportion of patients (10.8%) affected by the EPG using the risk-adjusted approach showed that the majority (88.9%) was older than 60 years when stratified by age. Unfortunately, specifications of terms concerning age such as «elderly» are vague and differ considerably depending on the source (24, 25, 33-35, 40). Therefore, we refrained from using a clear age threshold when assessing appropriateness of treatment. Nevertheless one should keep in mind that the observed EPG might further decrease dependent on the definition of the «elderly» used.

Besides age, but partially associated with age, there are other factors like patients' frailty, orthostatic hypotension, vertigo, social circumstances, individual compliance and preferences as well as comorbidities and preexisting polypharmacy that might influence the decision process. One faces the challenge of balancing advantages and disadvantages of every additional treatment based on these factors. Obviously, every additional treatment as well as every concomitant chronic disease will complicate the decision (41, 42). In this study, patients had a mean of 4.8 concomitant chronic diseases and received 5.9 concomitant drugs. These circumstances emphasize that more effectiveness studies in primary care are needed in order to define the evidence base of treatment, since multimorbid patients with concomitant polypharmacy are often excluded from guideline-influencing RCTs. One of the latest studies on the topic of BP management e.g. excluded patients affected by dementia, diabetes, history of stroke or those living in a nursing home that are commonly found in the primary care setting (43). This study among patients with high CVR targeting a SBP of less than 120 mm Hg, as compared with less than 140 mm Hg, resulted in lower rates of fatal and nonfatal major cardiovascular events and death from any cause, although the intensive-treatment group observed significantly higher rates of some adverse events (43, 44). These results, supported by data of a big meta-analysis, will influence future guidelines. Nevertheless the importance of risk-adjustment and patient centeredness holds true (45).

Strengths und limitations

In our dataset, the prevalence of hypertension is seemingly low compared to other studies in the primary care setting (9, 10, 14, 21, 46-48). This is explained by exclusion of patients who had less than two encounters and/or less than two BP measurements at their PCP. This decision was taken, because we aimed to specifically analyze PCPs' treatment performance, as it is unlikely that the PCP could have an influence on patients' hypertension treatment without regular contact. Leaving these patients within our analysis, the prevalence of patients with hypertension would have been 18.4%, and thus similar to other studies in this setting. Nevertheless our analysis is still based on data of 22'434 patients.

Our data are extracted from routinely collected data from medical records. Therefore, they are subject to the usual limitations of routine data (49, 50). We assessed patients' CVR profile according to the 2013 ESH/ESC guideline, but some variables (i.e. smoking, abdominal obesity, family history for premature

cardiovascular diseases and indicators for asymptomatic organ damage) were limited or not available in our dataset. One might define these shortcomings as a weakness of our study. However, PCPs base their daily decisions on the same variables as we did when extracting data from their medical records. Thus, these data are the best available proxy to measure the actual medical care situation of primary care patients with hypertension to date. A prospective study in this setting would be a disruption of daily practice and prone to the Hawthorne effect (51).

Further, one might see the cross-sectional view as a limitation, but it has to be acknowledged that data of previous studies derived from surveys where data collection usually took place on a single day. In contrast, we evaluated patients' qualifying for drug treatment based on the whole available record history.

This study on patients with hypertension in Swiss primary care is of international value as hypertension treatment is an eminent problem in health systems worldwide and the majority of patients with hypertension are treated in this setting (8; 9; 12; 43;). Most likely, our data cannot be generalized and directly transferred to other care settings, but countries with an equal health system should take these results as a hint to revisit previous EPG estimations. Switzerland serves as a good example of an industrialized country with an insurance based health care system with a fee-for-service reimbursement and mostly free choice of doctors – a model that can also be found in other countries, e.g. Austria, France or Germany and parts of the United States. The estimation of the actual risk-adjusted EPG in Swiss Primary Care will thus allow an extrapolation of the EPG in these countries.

Conclusion

Application of the risk-adjusted approach as recommended by the 2013 ESH/ESC guideline reduced the EPG by more than 50%. This shows the major impact of risk-adjustment and highlights the need for a patient centered approach in the treatment of patients with hypertension.

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Table 1. Definition of risk factors, asymptomatic organ damage and established disease.

Risk factors	Male sex	male sex
	Age	male sex and age ≥ 55 years or female sex and age ≥ 65 years (age assessed on date of study inclusion)
	Dyslipidemia	use of lipid-lowering-medication (ATC C10) or ICPC-2 Code (lipid disorder) or cholesterolin > 4.9 mmol/l or low density lipoprotein > 3.0 mmol/l or triglycerides > 1.7 mmol/l, or male sex and high density lipoprotein < 1.0 mmol/l or female sex and high density lipoprotein < 1.2 mmol/l
	Obesity	ICPC-2 Code (obesity) or BMI ≥ 30
	Elevated fasting glucose	fasting glucose level between 5.6 mmol/l and 6.9 mmol/l
Asymptomatic organ damage	Pulse pressure	difference between systolic and diastolic blood pressure ≥ 60 mmHg and age ≥ 65 years (age assessed on date of study inclusion)
	Chronic kidney disease Grade 3	glomerular filtration rate between 30 ml/min/1.73 m ² and 60 ml/min/1.73 m ² according to CKD-EPI formular *
Established disease	Chronic kidney disease Grade 4	glomerular filtration rate < 30 ml/min/1.73 m ² according to CKD-EPI formular *
	Diabetes	use of antidiabetic medication (ATC A10A, A10B, A10X) or ICPC-2 Code (diabetes insulin dependent, diabetes not insulin dependent) or at least two blood sugar measurements ≥ 7.0 mmol/l or HBA1C ≥ 6.5 %
	Cardiovascluar disease	use of cardiac medication (ATC C01) or ICPC-2 Code (ischaemic heart disease with angina, acute myocardial infarction, ischaemic heart disease with/without angina, heart failure, atrial fibrillation/flutter, paroxysmal tachykardia, transient cerebral ischaemia , stroke/cerebrovascular accident, cerebrovascular disease, atherosclerosis/PVD, retinopathy)

* CKD-EPI = Chronic Kidney Disease Epidemiology collaboration equation; glomerular filtration rate (GFR) = $141 \times \min(\text{Scr}/K, 1)^\alpha \times \max(\text{Scr}/K, 1)^{-1.209} \times 0.993^{\text{Age}} \times 1.018[\text{if female}] \times 1.159[\text{if black}]$; K = 0.7 if female and 0.9 if male; $\alpha = -0.329$ if female and -0.411 if male; min = The minimum of Scr/K or 1; max = The maximum of Scr/K or 1; Scr = serum creatinine (mg/dL). (28)

Table 2. Baseline characteristics of included patients

Characteristics	Included patients (n=22'434)	
	<i>mean</i>	<i>SD</i>
Age (years)	66.4	15.6
Observation period (years)	2.7	1.9
Antihypertensive drugs * (number per patient)	1,8	1.0
Concomitant drugs (number per patient)	5.9	5.9
Concomitant chronic diseases (number per patient)	4.8	3.7
Blood pressure measurements (total number per patient)	9.7	12.1
Blood pressure measurements (number per patient per year)	3.7	6.3
<u>Hypertension grade</u>	<i>n</i>	%
Normal (SBP ≤129 or DBP ≤84)	1'224	5.5%
High normal (SBP 130-139 or DBP 85-89)	4'900	21.8%
Grade 1 (SBP 140-159 or DBP 90-99)	12'672	56.5%
Grade 2 (SBP 160-179 or DBP 100-110)	3'118	13.9%
Grade 3 (SBP ≥180 or DBP ≥110)	520	2.3%
<u>Risk factors</u>	<i>n</i>	%
Male sex	11'364	50.7%
Age (male ≥55; female ≥65 years)	14'143	63.0%
Dyslipidemia	1'500	6.7%
Obesity	5'989	26.7%
Elevated fasting glucose **	74	22.6%
<u>Asymptomatic organ damage</u>	<i>n</i>	%
Pulse pressure ≥60mmHg (in patients ≥65 years)	12'736	56.8%
Chronic kidney disease Grade 3 ***	2'184	21.8%
<u>Established disease</u>	<i>n</i>	%
Chronic kidney disease Grade 4 ***	238	2.4%
Diabetes	918	4.1%
Cardiovascular disease	1'041	4.6%

* Data calculated only among patients with antihypertensive drugs
(n=13'506, 60.2% of 22'434)

** Data calculated only among patients where laboratory data was available
(n=328, 1,5% of 22'434)

*** Data calculated only among patients where laboratory data was available
(n=12'426, 55,4% of 22'434)

Other risk factors, asymptomatic organ damage or disease	Blood Pressure (mmHg)				
	Normal SBP \leq 129 or DBP \leq 84	High normal SBP 130-139 or DBP 85-89	Grade I HT SBP 140-159 or DBP 90-99	Grade II HT SBP 160-179 or DBP 100-109	Grade III HT SBP \geq 180 or DBP \geq 110
No other RF	• No BP intervention n = 116	• No BP intervention n = 423	Lifestyle changes for several months Then add BP drugs targeting <140/90 n=1265	• Lifestyle changes for several weeks • Then add BP drugs targeting < 140/90 n = 308	• Lifestyle changes • Immediate BP drugs targeting < 140/90 n = 44
1-2 RF	• No BP intervention n = 900	• Lifestyle changes • No BP Intervention n = 1224	• Lifestyle changes for several weeks • Then add BP drugs targeting < 140/90 n = 3554	• Lifestyle changes for several weeks • Then add BP drugs targeting < 140/90 n = 845	• Lifestyle changes • Immediate BP drugs targeting < 140/90 n = 141
\geq 3RF	• No BP intervention n = 208	• Lifestyle changes • No BP Intervention n = 147	• Lifestyle changes for several weeks • Then add BP drugs targeting < 140/90 n = 325	• Lifestyle changes • BP drugs targeting < 140/90 n = 247	• Lifestyle changes • Immediate BP drugs targeting < 140/90 n = 22
OD, CKD stage 3 or diabetes	• No BP intervention n = 0	• Lifestyle changes • No BP Intervention n = 2626	• Lifestyle changes • BP drugs targeting < 140/90 n = 6467	• Lifestyle changes • BP drugs targeting < 140/90 n = 1484	• Lifestyle changes • Immediate BP drugs targeting < 140/90 n = 272
Symptomatic CVD, CKD stage \geq 4 or diabetes with OD/RFs	• No BP intervention n = 0	• Lifestyle changes • No BP Intervention n = 480	• Lifestyle changes • P61BP drugs targeting < 140/90 n = 1061	• Lifestyle changes • BP drugs targeting < 140/90 n = 234	• Lifestyle changes • Immediate BP drugs targeting < 140/90 n = 41





